

BOOSTRIX™ POLIO

1. NAME OF THE MEDICINAL PRODUCT

boostrix™ polio

Diphtheria, tetanus, pertussis (acellular, component) and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 ml) contains:

Diphtheria toxoid¹ not less than 2 International Units (IU) (2.5 Lf)

Tetanus toxoid¹ not less than 20 International Units (IU) (5 Lf)

Bordetella pertussis antigens

Pertussis toxoid¹ 8 micrograms

Filamentous Haemagglutinin¹ 8 micrograms

Pertactin¹ 2.5 micrograms

Inactivated poliovirus

type 1 (Mahoney strain)² 40 D-antigen unit

type 2 (MEF-1 strain)² 8 D-antigen unit

type 3 (Saukett strain)² 32 D-antigen unit

¹adsorbed on aluminium hydroxide, hydrated (Al(OH)₃) 0.3 milligrams Al³⁺
and aluminium phosphate (AlPO₄) 0.2 milligrams Al³⁺

²propagated in VERO cells

boostrix™ polio is a turbid white suspension. Upon storage, a white deposit and clear supernatant can be observed. This is a normal finding.

3. PHARMACEUTICAL FORM

Suspension for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

boostrix™ polio is indicated for booster vaccination against diphtheria, tetanus, pertussis and poliomyelitis of individuals from the age of three years onwards.

boostrix™ polio is not intended for primary immunisation of children below the age of 3 years.

4.2 Posology and Method of Administration

Posology

A single 0.5 ml dose of the vaccine is recommended.

boostrix™ polio may be administered from the age of three years onwards. *boostrix™ polio* should be administered in accordance with official recommendations and/or local practice regarding the use of vaccines with reduced content of diphtheria toxoid plus tetanus toxoid in combination with pertussis and poliomyelitis antigens.

Boostrix™ Polio may be administered to adolescents and adults with unknown vaccination status or incomplete vaccination against diphtheria, tetanus and pertussis as part of an immunisation series against diphtheria, tetanus, pertussis and polio (see *Pharmacodynamics*).

Based on data in adults, two additional doses of a diphtheria and tetanus containing vaccine are recommended one and six months after the first dose to maximize the vaccine response against diphtheria and tetanus. *boostrix™ polio* can be used in the management of tetanus prone injuries in persons who have previously received a primary vaccination series of tetanus toxoid vaccine. Tetanus immunoglobulin should be administered concomitantly in accordance with official recommendations.

Repeat vaccination against diphtheria, tetanus, pertussis and poliomyelitis should be performed at intervals as per official recommendations (generally 10 years).

Method of administration

boostrix™ polio is for deep intramuscular injection, preferably in the deltoid region (see also 4.4 Special Warnings and Special Precautions for Use).

4.3 Contra-indications

boostrix™ polio should not be administered to subjects with known hypersensitivity to any component of the vaccine (see sections 2 Qualitative and Quantitative Composition and 6.1 List of Excipients) or to subjects having shown signs of hypersensitivity after previous administration of diphtheria, tetanus, pertussis or poliomyelitis vaccines.

boostrix™ polio is contra-indicated if the subject has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis-containing vaccine. In these circumstances, pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria, tetanus and poliomyelitis vaccines.

boostrix™ polio should not be administered to subjects who have experienced neurological complications following an earlier immunisation against diphtheria and/or tetanus (for convulsions or hypotonic-hyporesponsive episodes, see section 4.4 Special Warnings and Special Precautions for Use).

4.4 Special Warnings and Special Precautions for Use

It is good clinical practice that vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic reaction following the administration of the vaccine.

As with other vaccines, administration of *boostrix™ polio* should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection is not a contraindication.

If any of the following events have occurred in temporal relation to receipt of pertussis-containing vaccine in infancy, the decision to give subsequent doses of pertussis-containing vaccines should be carefully considered.

- Temperature of $\geq 40.0^{\circ}\text{C}$ (rectal) within 48 hours of vaccination, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours of vaccination.
- Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks, particularly since these events are not associated with permanent sequelae. According to available clinical data, the risk of such reactions is lower with acellular pertussis vaccines than with whole cell pertussis vaccines.

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunisation until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.

***boostrix™ polio* should in no circumstances be administered intravascularly.**

boostrix™ polio should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects. Firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

Collapse or shock-like state (hypotonic-hyporesponsive episode) and convulsions have been reported very rarely following immunisation of children with products containing one or more of the antigenic constituents of *boostrix™ polio*.

A history of febrile convulsions, a family history of convulsions, a family history of Sudden Infant Death Syndrome (SIDS) and a family history of an adverse event following DTP vaccination do not constitute contra-indications.

Human Immunodeficiency Virus (HIV) infection is not considered as a contra-indication.

The expected immunological response may not be obtained after vaccination of immunosuppressed patients e.g. patients on immunosuppressive therapy.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Boostrix™ Polio can be given concomitantly with any of the following monovalent or combination vaccines: measles, mumps, rubella, varicella and human papilloma virus vaccine (see *Adverse Reactions*).

Concomitant use with other inactivated vaccines and with immunoglobulin is unlikely to result in interference with the immune responses.

If *boostrix™ polio* is to be given at the same time as another injectable vaccine or immunoglobulin, the products should always be given at different sites.

As with other vaccines, it may be expected that in patients receiving immunosuppressive therapy or patients with immunodeficiency an adequate immunologic response may not be achieved.

4.6 Pregnancy and Lactation

Fertility

No human data available. Animal studies do not indicate direct or indirect harmful effects with respect to female fertility (see section 5.2 Pre-clinical Safety Data).

Pregnancy

Safety data from a prospective observational study where **Boostrix™** (dTpa component of **Boostrix™ Polio**) was administered to pregnant women during the third trimester (793 pregnancy outcomes) as well as data from post-marketing surveillance where pregnant women were exposed to **Boostrix™ Polio** or to **Boostrix™** have shown no vaccine related adverse effect on pregnancy or on the health of the foetus/newborn child.

As with other inactivated vaccines, it is not expected that the polio antigens contained in **Boostrix™ Polio** would harm the foetus.

The use of **Boostrix™ Polio** may be considered during the third trimester of pregnancy.

Human data from prospective clinical studies on the use of **Boostrix™ Polio** during the first and second trimester of pregnancy are not available.

Limited data indicate that maternal antibodies may reduce the magnitude of the immune response to some vaccines in infants born from mothers vaccinated with **Boostrix™ Polio** during pregnancy. The clinical relevance of this observation is unknown.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or post-natal development (see section Pre-clinical Safety Data).

Boostrix™ Polio should only be used during pregnancy when the possible advantages outweigh the possible risks for the foetus.

Lactation
The safety of **boostrix™ polio** when administered to breast-feeding women has not been evaluated.

It is unknown whether **boostrix™ polio** is excreted in human breast milk.

boostrix™ polio should only be used during breast-feeding when the possible advantages outweigh the potential risks.

4.7 Effects on Ability to Drive and Use Machines

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

4.8 Undesirable Effects

Clinical Trials Data

The safety profile presented in Table 1 is based on data from clinical trials where **boostrix™ polio** was administered to 908 children (from 4 to 9 years of age) and 955 adults, adolescents and children (above 10 years of age).

The most common events occurring after vaccine administration in both groups were local injection site reactions (pain, redness and swelling) reported by 31.3 – 82.3% of subjects overall. These had their onset within the first day after vaccination. All resolved without sequelae.

Adverse reactions reported are listed according to the following frequency:

Very common: $\geq 1/10$

Common: $\geq 1/100$ and $< 1/10$

Uncommon: $\geq 1/1,000$ and $< 1/100$

Rare: $\geq 1/10,000$ and $< 1/1,000$

Very rare: $< 1/10,000$

Table 1: Adverse reactions reported in clinical trials with *Boostrix™ Polio*

<i>System Organ Class</i>	<i>Frequency</i>	<i>Adverse reactions</i>	
		<i>Children from 4 to 9 years of age</i>	<i>Adults, adolescents and children from the age of 10 years onwards</i>
<i>Infections and infestations</i>	Uncommon		oral herpes
<i>Blood and lymphatic system disorders</i>	Uncommon	lymphadenopathy	lymphadenopathy
<i>Metabolism and nutrition disorders</i>	Common	anorexia	
	Uncommon		decreased appetite
<i>Psychiatric disorders</i>	Common	irritability	
	Uncommon	sleep disorder, apathy	
<i>Nervous system disorders</i>	Very common	somnolence	headache
	Common	headache	
	Uncommon		paraesthesia, somnolence, dizziness
<i>Respiratory, thoracic and mediastinal disorders</i>	Uncommon	dry throat	asthma
<i>Gastrointestinal disorders</i>	Common		gastrointestinal disorders
	Uncommon	diarrhoea, vomiting, abdominal pain, nausea	
<i>Skin and subcutaneous tissue disorders</i>	Uncommon		pruritus
<i>Musculoskeletal and connective tissue disorders</i>	Uncommon		myalgia, arthralgia
<i>General disorders and administration site conditions</i>	Very common	injection site reactions (including pain, redness and swelling)	injection site reactions (including pain, redness and swelling), fatigue

	Common	fever ≥ 37.5 °C (including fever > 39 °C), injection site reactions (such as haemorrhage)	fever ≥ 37.5 °C, injection site reactions (such as haematoma)
	Uncommon	fatigue	fever > 39 °C, chills, pain

Coadministration with MMR/V vaccines in children aged 3-6 years

Boostrix™ Polio was coadministered with MMR/V vaccines in 2 clinical studies with 406 children aged 3-6 years. In these studies, upper respiratory tract infection and rash were commonly reported. Fever, irritability, fatigue, loss of appetite and gastrointestinal disorders (including diarrhoea and vomiting) were reported with a higher frequency (very common) when compared to Table 1 while all other adverse reactions occurred at the same or lower frequency.

Adverse reactions additionally reported during clinical studies with **Boostrix™** (dTpa component of **Boostrix™ Polio**), administered to 839 children (from 4 to 9 years of age) and 1,931 adults, adolescents and children (above 10 years of age), are listed in Table 2:

Table 2: Adverse reactions reported in clinical trials with **Boostrix™**

<i>System Organ Class</i>	<i>Frequency</i>	<i>Adverse reactions</i>	
		<i>Children from 4 to 9 years of age</i>	<i>Adults, adolescents and children from the age of 10 years onwards</i>
<i>Infections and infestations</i>	Uncommon		upper respiratory tract infection, pharyngitis
<i>Nervous system disorders</i>	Uncommon	disturbances in attention	syncope
<i>Eye disorders</i>	Uncommon	conjunctivitis	
<i>Respiratory, thoracic and mediastinal disorders</i>	Uncommon		cough
<i>Gastrointestinal disorders</i>	Common		nausea
	Uncommon		diarrhoea, vomiting
<i>Skin and subcutaneous tissue disorders</i>	Uncommon		hyperhidrosis, rash
<i>Musculoskeletal and connective tissue disorders</i>	Uncommon		joint stiffness, musculoskeletal stiffness
<i>General disorders and administration site conditions</i>	Very common		malaise
	Common		injection site reactions (such as injection site mass and injection site abscess sterile)

	Uncommon	injection site reactions (such as induration), pain	influenza like illness
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*Reactogenicity after repeat dose of **Boostrix™ Polio** or **Boostrix™***

Subjects fully primed with 4 doses of DTPa followed by **boostrix™ polio** at around 4-8 years of age show no increased reactogenicity after the second **boostrix™ polio** dose administered 5 years later.

Subjects aged 15 years onwards without recent vaccination for diphtheria, tetanus, pertussis and polio, who received a dose of **Boostrix™ Polio** or another reduced-antigen content vaccine, followed by an additional dose of **Boostrix™ Polio** 10 years after, showed no increased reactogenicity.

Subjects fully primed with 4 doses of DTPw followed by a **Boostrix™** dose around 10 years of age show an increase of local reactogenicity after an additional **Boostrix™** dose administered 10 years later.

Post-Marketing Data

Table 3: Adverse reactions reported with **Boostrix™ Polio** during post-marketing surveillance

<i>System Organ Class</i>	<i>Frequency</i>	<i>Adverse reactions</i>
<i>Blood and lymphatic system disorders</i>	Rare	angioedema
<i>Immune system disorders</i>	Very rare	allergic reactions, including anaphylactic and anaphylactoid reactions
<i>Nervous system disorders</i>	Rare	convulsions (with or without fever)
<i>Skin and subcutaneous tissue disorders</i>	Rare	urticaria
<i>General disorders and administration site conditions</i>	Rare	extensive swelling of the vaccinated limb, asthenia

4.9 Overdose

Cases of overdose have been reported during post-marketing surveillance. Adverse events following overdosage, when reported, were similar to those reported with normal vaccine administration.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA02

Immune response

The following immune responses were observed across studies one month post vaccination with **Boostrix™ Polio** in children, adolescents and adults (Table 4).

Table 4: Immune response in children, adolescents and adults

Antigen	Response	Children aged 3 to 9 years N=1195 (% vaccinees)	Adults, adolescents and children aged from 10 years onwards N=923 (% vaccinees)
Diphtheria	≥ 0.1 IU/ml	100%	82.2 – 100%
Tetanus	≥ 0.1 IU/ml	99.9 – 100%	99.6 – 100%
Pertussis			
Pertussis toxoid	Booster response*	84.6 – 90.6%	79.8 – 94.0%
Filamentous haemagglutinin		90.1 – 98.8%	90.7 – 97.2%
Pertactin		94.2 – 96.6%	90.0 – 96.7%
Inactivated poliovirus			
type 1	≥8 ED50	98.8 – 100%	99.6 – 100%
type 2		99.2 – 100%	99.6 – 100%
type 3		99.4 – 100%	99.1 – 100%

N=number of subjects

*Booster response defined as:

- for initially seronegative subjects, antibody concentrations at least four times the cut-off (post-vaccination concentration ≥ 20 EI.U/ml);
- for initially seropositive subjects with Pre booster vaccination concentration ≥ 5 EI.U/ml and < 20 EI.U/ml: an increase in antibody concentrations of at least four times the Pre booster vaccination concentration.
- for initially seropositive subjects with Pre booster vaccination concentration ≥ 20 EI.U/ml: an increase in antibody concentrations of at least two times the Pre booster vaccination concentration

As with other adult-type Td vaccines, **boostrix™ polio** induces higher seroprotection rates and higher titres of both anti-D and anti-T antibodies in children and adolescents as compared to adults.

Efficacy in protecting against pertussis

The pertussis antigens contained in **boostrix™ polio** are an integral part of the paediatric acellular pertussis combination vaccine (**Infanrix™**), for which efficacy after primary vaccination has been demonstrated in a household contact efficacy study. The antibody titres to all three pertussis components following vaccination with **boostrix™ polio** are at least as high or higher than those observed during the household contact efficacy trial. Based on these comparisons, **boostrix™ polio** would provide protection against pertussis, however the degree and duration of protection afforded by the vaccine are undetermined.

Persistence of the immune response

The following seroprotection/seropositivity rates were observed five years after vaccination with **Boostrix™ Polio** in children and 10 years after vaccination with **Boostrix™ Polio** in adolescents and adults (Table 5).

Table 5: Persistence of immune response in children, adolescents and adults

Antigen	Seroprotection/ seropositivity	5 years after vaccination of children (aged 4-8 years) (N=344) (% vaccinees)	10 years after vaccination of adolescents and adults (aged 15 years onwards) (N=201) (% vaccinees)
Diphtheria	≥ 0.1 IU/ml	89.4%*	81.0%**
Tetanus	≥ 0.1 IU/ml	98.5%	98.4%
Pertussis			
Pertussis toxoid	≥ 5 EL.U/ml	40.9%	78.7%
Filamentous haemagglutinin		99.7%	100%
Pertactin		97.1%	88.7%
Inactivated poliovirus			
type 1	≥ 8 ED50	98.8%	100%
type 2		99.7%	100%
type 3		97.1%	98.3%

*98.2% of subjects with antibody concentrations associated with protection against disease ≥ 0.016 IU/ml by an *in-vitro* Vero-cell neutralisation assay.

**92.1% of subjects with antibody concentrations associated with protection against disease ≥ 0.01 IU/ml by an *in-vitro* Vero-cell neutralisation assay.

*Immune response after a repeat dose of **Boostrix™ Polio***

The immunogenicity of **boostrix™ polio**, administered 5 years after a previous booster dose of **boostrix™ polio** at 4 to 8 years of age, has been evaluated. One month post vaccination, > 99 % of subjects were seropositive against pertussis and seroprotected against diphtheria, tetanus and all three polio types.

In adults, one dose of **Boostrix™ Polio** administered 10 years after the previous dose, elicited a protective immune response in > 96.8% of the subjects (for the diphtheria antigen) and in 100% of the subjects (for the tetanus and polio antigens). The booster response against the pertussis antigens was between 74.2 and 98.4%.

Immune response in subjects without prior or with unknown vaccination history

In adolescents aged from 11 to 18 years, without previous pertussis vaccination and no vaccination against diphtheria and tetanus in the previous 5 years, one dose of **Boostrix™** (dTpa component of **Boostrix™ Polio**) induced an antibody response against pertussis and all subjects were protected against tetanus and diphtheria.

In subjects ≥ 40 years of age that had not received any diphtheria or tetanus containing vaccine in the past 20 years (including those who have never been vaccinated or whose vaccination

status was unknown), one dose of *boostrix*TM *polio* induced an antibody response against pertussis and protected against tetanus and diphtheria in the majority of cases.

5.2 Preclinical Safety Data

Reproductive toxicology

Fertility

Non-clinical data obtained with *boostrix*TM *polio* reveal no specific hazard for humans based on conventional studies of female fertility in rats and rabbits.

Pregnancy

Non-clinical data obtained with *boostrix*TM *polio* reveal no specific hazard for humans based on conventional studies of embryo-foetal development in rats and rabbits, and also of parturition and postnatal toxicity in rats (up to the end of the lactation period).

Animal toxicology and/or pharmacology

Preclinical data reveal no special hazard for humans based on conventional studies of safety and of toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Medium 199 (as stabilizer), sodium chloride, water for injections, Formaldehyde, polysorbate 80, neomycin sulfate, polymyxin B sulfate are present as residues from the manufacturing process.

6.2 Incompatibilities

*boostrix*TM *polio* should not be mixed with other vaccines in the same syringe.

6.3 Shelf Life

The expiry date is indicated on the label and packaging.

6.4 Special Precautions for Storage

*boostrix*TM *polio* should be stored at +2°C to +8°C.

Do not freeze. Discard if the vaccine has been frozen.

6.5 Nature and Contents of Container

Suspension for injection in pre-filled syringes or glass vials (Type I glass) (0.5 ml) with rubber stoppers.

Not all presentations are available in every country.

6.6 Instructions for Use and Handling

Prior to use, the vaccine should be at room temperature and well shaken in order to obtain a homogeneous turbid white suspension. Prior to administration, the vaccine should be visually inspected for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the vaccine.

Upon removal from refrigerator, the vaccine is stable for 8 hours at + 21°C.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Thailand) Ltd.

8. MARKETING AUTHORISATION NUMBER

2C 14/50 (NB)

9. DATE OF FIRST AUTHORISATION

3 Jul 2007 (conditional license)

12 Apr 2010 (unconditional license)

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